

METHODS AND REAGENTS FOR REGULATING OBESITY

Abstract of the Invention

Lines of transgenic mice have been developed which preferentially express a syndecan in the regions of the hypothalamus which are known to be important in weight control. The animals were made using a construct including a cytomegalovirus promoter and the 3' untranslated region, including the polyadenylation site, of the bovine growth hormone gene, as well as cDNA encoding syndecan-1. The mice express the syndecan-1 transgene in many tissues, with expression in the brain occurring preferentially in their hypothalamus. The mice are characterized by elevated levels of circulating syndecan-1 ectodomain and exhibit enormous weight gain after reaching sexual maturity. Transgenic animals in which stop codons have been inserted into the construct so that the syndecan is not expressed do not exhibit the same enormous weight gain. The animals have a relatively normal distribution of fat, are completely healthy and heterozygotes reproduce, and show other indicators associated with obesity in humans. The mice are useful in understanding the factors involved in weight regulation and in designing and screening for drugs which are involved in weight regulation and that can either enhance or reduce appetite and activity.